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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,800	06/26/2003	Junji Hamuro	238027US0CONT	7806

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EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/603,800	HAMURO ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-20 are pending in the present application.

Applicant's election with traverse of the following species: (a) macrophages as a cell species; (b) N,N'-diacylcystine as a species of a substance; and (c) corneal epithelium as a species of an organ, in reply filed on 12/23/04 is acknowledged. The traversal is on the ground(s) that the Office has not provided any reasons or examples to support a conclusion that the species are indeed patentably distinct, and that a search of all the claims would not impose a serious burden on the Office.

This is not found persuasive because with respect to Applicants' latter argument, claims 1-20 are being examined on the merits with respect to the elected species. With respect to Applicants' traverse on species restriction, as noted in the previous Office action mailed on 11/30/04, should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention. Since Applicant fails to submit evidence or identify such evidence, the species are distinct.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 1-20 are examined on the merits herein, with (a) macrophages as a cell species; (b) N,N'-diacylcystine as a species of a substance; and (c) corneal epithelium as a species of an organ.

Information Disclosure Statement

Related cases listed in the IDS dated 10/03/03 and the English translation of the International Preliminary Report listed in the IDS dated 1/07/04 have been considered by the Examiner. However, there are no attached PTO 1449 for these information disclosure statments.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamuro et al. (EP 1 004 302 A2, IDS).

With respect to the elected species, claims 1-8 are drawn to a composition comprising N, N'-diacylcystine as an active ingredient that has a function of decreasing a reduced glutathione content in macrophages; claims 9-10 and 12 are directed to a pharmaceutical composition comprising the same composition and a food, drink or nutriment preparation comprising the same, respectively. **Please note that for a composition claim, its intended use is not given any patentable weight in light of the prior art.** Claim 11 is drawn to a method of decreasing a reduced glutathione content in macrophages comprising administering the composition of claim 1 to the

cells. Claims 13-17 are directed to a method of suppressing, alleviating, reducing, treating, and retarding transplant rejection in a subject, comprising administering the composition of claim 1 to the subject. Claim 20 is drawn to a method of making a composition comprising contacting N, N'-diacylcystine that has a function of decreasing a reduced glutathione content in macrophages, as an active ingredient and a pharmaceutically acceptable carrier.

Hamuro et al already disclose N, N'-diacetylcystine [$(NAC)_2$] to be a substance having the activity of reducing the content of reductive glutathione in the macrophages (page 9, paragraphs 49-51; page 5, paragraph 21), and that this immunomodulator can be included in a drug, a food (e.g., food for medical care, a health food or a special sanitary food, a toothpaste, a chewing gum and the like), a nutrient (e.g., vitamin and calcium preparations) and an infusion such as a high calory infusion, a physiological saline solution and blood preparations (see abstract; page 2, paragraphs 1-2; page 3, paragraph 10; page 6, paragraph 22). Please not that a physiological saline solution, a high calory infusion, a chewing gum is considered to be a pharmaceutically acceptable carrier. Hamuro et al further teach the immunomodulator is useful as an immunosuppressant against human immunological diseases such as inflammatory bowel diseases (e.g., ulcerative colitis and Crohn disease) and gastrointestinal inflammatory diseases such as hepatitis and hepatic cirrhosis (see abstract). Hamuro et al also disclose that the immunomodulator can be applied not only to patients suffering from attacked or chronic diseases but also to high-risk persons suffering from adult diseases (page 10, last sentence of paragraph 57). The dose of the substance

having an activity of changing the content of reductive glutathione as an active ingredient, $(NAC)_2$ for this instance, is selected depending on the conditions of the patients or the like to which the substance is administered or the use purpose, including the dosage between 1 and 5,000 mg (oral drug), preferably between 10 and 500 mg/day, which is within the recited dose ranging from 1 mg to 10 g (page 10, top of paragraph 54). Non-limited examples showed that $(NAC)_2$ was administered intraperitoneally at 20 ug/0.5ml/h each for 20 h in mice on day 1 and day 2 to induce oxidative macrophages (example 9), and that the administration of $(NAC)_2$ inhibits delayed type hypersensitivity reaction to ovalbumin (example 10), inhibits spontaneous inflammatory bowel diseases in γc knockout mice having intestinal inflammation similar to that of humans (example 13) and suppress joint swelling in a rat adjuvant-induced arthritis (example 19).

Since a composition comprising $(NAC)_2$ in the form of a drug, a food, a nutrient or an infusion taught by Hamuro et al. is indistinguishable from the elected composition of the present invention, the reference anticipates the instant composition claims. The teachings of Hamuro et al. also meet every limitation of the methods in claims 11 and 20 (see the above teachings). With respect to claims 13-18, please note that the claims merely recite a single step of administering the composition containing the elected $(NAC)_2$ in any subject (the subject does not need or even receive any transplant), and therefore the teachings of Hamuro et al for administering $(NAC)_2$ in a patient to treat human immunological diseases such as inflammatory bowel diseases (e.g., ulcerative

colitis and Crohn disease) and gastrointestinal inflammatory diseases such as hepatitis and hepatic cirrhosis also meet every limitation of the method as claimed.

Accordingly, the reference anticipates the instant claims as written.

Conclusions

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (571) 272-0767, or SPE, Irem Yucel, Ph.D., at (571) 272-0781.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Quang Nguyen, Ph.D.